

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 10:04:35 ON 12 SEP 2003

L1 68729 S ADENOVIRUS  
L2 33610 S CAPSID  
L3 1229238 S CAPSID OR SURFACE  
L4 1618251 S NON-NATIVE OR LIGAND OR ANTIGEN  
L5 255601 S L4 AND L3  
L6 1647 S L1 AND L5  
L7 11 S NON(W)NATIVE LIGAND  
L8 0 S L7 AND L1  
L9 350229 S LIGAND  
L10 362 S L1 AND L3 AND L9  
L11 183 DUP REM L10 (179 DUPLICATES REMOVED)  
L12 967236 S REPLAC? OR RECOMBINANT  
L13 4530 S L1 AND L3  
L14 1293 S L12 AND L13  
L15 142 S L9 AND L14  
L16 74 DUP REM L15 (68 DUPLICATES REMOVED)  
L17 1305534 S ANTIGEN  
L18 1366 S L13 AND L17  
L19 217479 S ANTIGEN? AND SURFACE  
L20 1053 S L1 AND L19  
L21 33610 S CAPSID  
L22 52 S L20 AND L21  
L23 40 DUP REM L22 (12 DUPLICATES REMOVED)

L16 ANSWER 50 OF 74 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN

ACCESSION NUMBER: 2001089480 EMBASE

TITLE: Targetable gene delivery vectors.

AUTHOR: Hallenbeck P.L.; Stevenson S.C.

SOURCE: Advances in Experimental Medicine and Biology, (2000) 465/-  
(37-46).

Refs: 49

ISSN: 0065-2598 CODEN: AEMBAP

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 004 Microbiology

016 Cancer

022 Human Genetics

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Adenoviral vectors, which have targeting **ligands** for tumor cells on the **capsid**, no natural tropism, and carry a therapeutic payload should be constructed soon and tested in pre-clinical models. Nevertheless, there are still important considerations for the design and therapeutic use of targetable vectors. Perhaps the single greatest challenge in the future, as it was in the past, will be finding **ligands** that have a higher apparent affinity for tumor and/or tumor endothelial cells than normal cells. However, the advent of many rapidly advancing technologies and information including the sequencing of the human genome, in vivo and in vitro phage display, rapid analysis of gene and protein expression in any context, and new cellular targets such as angiogenic endothelial cells, may provide many opportunities for the discovery of novel and useful **ligands**. In addition, the interests in targeting vectors are rapidly growing with new journals and meetings solely devoted to this subject increasing annually. Within the next 5 years, we should have meaningful clinical data on targetable vectors to reassess our progress.

DOCUMENT NUMBER: 99362675 PubMed ID: 10430860  
TITLE: Redirected infection of directly biotinylated  
**recombinant adenovirus** vectors through  
cell **surface** receptors and antigens.  
AUTHOR: Smith J S; Keller J R; Lohrey N C; McCauslin C S; Ortiz M;  
Cowan K; Spence S E  
CORPORATE SOURCE: Laboratories of Molecular Immunoregulation, National Cancer  
Institute-Frederick Cancer Research and Development Center,  
Frederick, MD 21702, USA.  
CONTRACT NUMBER: NO1-CO-56000 (NCI)  
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE  
UNITED STATES OF AMERICA, (1999 Aug 3) 96 (16) 8855-60.  
Journal code: 7505876. ISSN: 0027-8424.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199909  
ENTRY DATE: Entered STN: 19990925  
Last Updated on STN: 20000303  
Entered Medline: 19990909

AB The inability of **adenovirus** to infect primitive hematopoietic cells presents an obstacle to the use of **adenovirus** vectors for gene transfer to these cell types. Therefore, expanding the tropism of **adenovirus** vectors to unique cell **surface** antigens would be an important development for gene therapy protocols. In this study, we sought to redirect infection of **adenovirus** vectors to primitive human hematopoietic cells that universally express the c-Kit receptor on their cell **surface**. To accomplish this, a vector was constructed by covalently linking biotin molecules to **recombinant adenovirus**, followed by addition of the biotinylated **ligand** for the c-Kit receptor, stem cell factor (SCF), through an avidin bridge. Gene transfer was directed specifically to c-Kit-positive hematopoietic cell lines, resulting in up to a 2,440-fold increase in luciferase expression with frequencies equivalent to **recombinant virus** infection of permissive cells. Substitution of biotinylated antibodies directed against c-Kit, CD34 (binds L-selectin), and CD44 (hyaluronate receptor) receptors for biotinylated SCF resulted in 50-, 8-, and 260-fold increases in reporter gene expression, respectively, demonstrating that infection also could be redirected through antibody-antigen interactions and through antigens other than growth factor receptors. The versatility of this vector was demonstrated further by infection of primary T cells with vectors targeted with antibodies to CD44 (resting and activated T cells) and biotinylated IL-2 (activated T cells only). Taken together, directly biotinylated **adenovirus** vectors represent a versatile and efficient method for redirection of virus infection to specific cells.

L16 ANSWER 63 OF 74 MEDLINE on STN DUPLICATE 31

ACCESSION NUMBER: 1998298563 MEDLINE  
DOCUMENT NUMBER: 98298563 PubMed ID: 9634824  
TITLE: Targeted gene delivery by tropism-modified adenoviral  
vectors.  
AUTHOR: Douglas J T; Rogers B E; Rosenfeld M E; Michael S I; Feng  
M; Curiel D T  
CORPORATE SOURCE: Gene Therapy Program, University of Alabama at Birmingham  
35294, USA.  
CONTRACT NUMBER: R01 5025505  
SOURCE: NATURE BIOTECHNOLOGY, (1996 Nov) 14 (11) 1574-8.  
Journal code: 9604648. ISSN: 1087-0156.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199808  
ENTRY DATE: Entered STN: 19980828  
Last Updated on STN: 19980828  
Entered Medline: 19980814

AB The utility of adenoviral vectors for gene therapy is currently limited due, in part, to the widespread distribution of the cellular receptor for the **adenovirus** fiber that precludes the targeting of specific cell types. In order to develop a targeted **adenovirus**, it is therefore necessary both to ablate endogenous viral tropism and to introduce novel tropism. We hypothesized that these two goals could be achieved by employing a neutralizing anti-fiber antibody, or antibody fragment, chemically conjugated to a cell-specific **ligand**. To test this concept, we chose to target the folate receptor, which is overexpressed on the **surface** of a variety of malignant cells. Therefore, we conjugated folate to the neutralizing Fab fragment of an anti-fiber monoclonal antibody. This Fab-folate conjugate was complexed with an adenoviral vector carrying the luciferase reporter gene and was shown to redirect adenoviral infection of target cells via the folate receptor at a high efficiency. Furthermore, when complexed with an adenoviral vector carrying the gene for herpes simplex virus thymidine kinase, the Fab-folate conjugate mediated the specific killing of cells that overexpress the folate receptor. This work thus represents the first demonstration of the retargeting of a **recombinant** adenoviral vector via a non-adenoviral cellular receptor.

L23 ANSWER 16 OF 40 MEDLINE on STN

ACCESSION NUMBER: 1999422052 MEDLINE

DOCUMENT NUMBER: 99422052 PubMed ID: 10490760

TITLE: Cocksackie and **adenovirus** receptor (CAR)-dependent and major histocompatibility complex (MHC) class I-independent uptake of recombinant **adenoviruses** into human tumour cells.

COMMENT: Comment in: Gene Ther. 1999 Sep;6(9):1497-8

AUTHOR: McDonald D; Stockwin L; Matzow T; Blair Zajdel M E; Blair G E

CORPORATE SOURCE: School of Biochemistry and Molecular Biology, University of Leeds, Leeds LS2 9JT, UK.

SOURCE: GENE THERAPY, (1999 Sep) 6 (9) 1512-9.  
Journal code: 9421525. ISSN: 0969-7128.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200004

ENTRY DATE: Entered STN: 20000413  
Last Updated on STN: 20021217  
Entered Medline: 20000403

AB The role of two receptors, previously proposed to mediate the entry of **adenoviruses** into human cells, the coxsackie and **adenovirus** receptor (CAR) and the major histocompatibility complex (MHC) class I heavy chain has been investigated. The expression of MHC class I in many tumours is reduced or absent, therefore if this were a means by which **adenoviruses** gained entry into cells, it would have important implications for their application in cancer treatment. In order to determine if MHC class I heavy chain is involved in **adenovirus** type 5 (Ad5) uptake, the binding of recombinant Ad5 fibre knob domain (which mediates viral attachment) to human cell lines that had greatly different levels of **surface** MHC class I was studied. We also created derivatives of a non-permissive Chinese hamster ovary (CHO) cell line that expressed human class I (HLA-A2) and found that these cells did not bind fibre or take up virus. In addition, the extracellular domain of CAR was expressed in E. coli and used to generate a polyclonal anti-CAR antibody. This antibody blocked both 125I labelled fibre knob binding and virus uptake. Thus CAR, and not MHC class I, is a receptor for human **adenoviruses** in cultured tumour cells. Tissue CAR levels may therefore be an important factor in the efficiency of **adenovirus**-mediated gene therapy.

L23 ANSWER 19 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN

ACCESSION NUMBER: 1998322054 EMBASE

TITLE: Development of novel cell **surface** CD34-targeted recombinant adenoassociated virus vectors for gene therapy.

AUTHOR: Yang Q.; Mamounas M.; Yu G.; Kennedy S.; Leaker B.; Merson J.; Wong-Staal F.; Yu M.; Barber J.R.

CORPORATE SOURCE: Dr. J.R. Barber, Immusol, Inc., 3050 Science Park Road, San Diego, CA 92121, United States

SOURCE: Human Gene Therapy, (1 Sep 1998) 9/13 (1929-1937).

Refs: 25

ISSN: 1043-0342 CODEN: HGTHE3

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology  
022 Human Genetics

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Recombinant adenoassociated virus (rAAV) type 2 vectors have been used to transduce a wide variety of cell types, including hematopoietic progenitor cells. For in vivo gene transfer, it is desirable to have an rAAV vector that specifically transduces selected target cells. As a first step toward generating an rAAV vector capable of targeting delivery in vivo, we have engineered a chimeric protein combining the AAV **capsid** protein and the variable region of a single-chain antibody against human CD34 molecules, a cell **surface** marker for hematopoietic stem/progenitor cells. Inclusion of the chimeric CD34 single-chain antibody-AAV **capsid** proteins within an rAAV virion significantly increased the preferential infectivity of rAAV for the CD34+ human myoleukemia cell line KG-1, which is normally refractory to rAAV transduction. Antibodies against the single-chain antibody and the CD34 protein blocked this transduction. This chimeric vector represents a significant improvement in the host range of rAAV and the first step toward specific gene delivery by rAAV vectors to cells of choice, in this case, hematopoietic progenitor cells, for the treatment of human disease.

L23 ANSWER 28 OF 40 MEDLINE on STN DUPLICATE 4  
ACCESSION NUMBER: 94157452 MEDLINE  
DOCUMENT NUMBER: 94157452 PubMed ID: 7509367  
TITLE: Expression of a foreign epitope on the **surface** of  
the **adenovirus** hexon.  
AUTHOR: Crompton J; Toogood C I; Wallis N; Hay R T  
CORPORATE SOURCE: Division of Cell and Molecular Biology, School of  
Biological and Medical Sciences, University of St Andrews,  
Fife, U.K.  
SOURCE: JOURNAL OF GENERAL VIROLOGY, (1994 Jan) 75 ( Pt 1) 133-9.  
Journal code: 0077340. ISSN: 0022-1317.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199403  
ENTRY DATE: Entered STN: 19940406  
Last Updated on STN: 19970203  
Entered Medline: 19940329

AB To present short protein sequences to the host immune system a foreign  
epitope has been expressed on the **surface** of the  
**adenovirus** virion as part of the hexon. As the trimeric hexon  
constitutes 240 out of the 252 capsomers of the virus, the foreign epitope  
is repeated 720 times on the virion **surface**. An eight amino  
acid sequence from the major **antigenic** site in the VP1  
**capsid** protein of poliovirus type 3 was engineered into two  
regions of the **adenovirus** type 2 hexon. The two loop regions  
chosen to accommodate the foreign sequences are exposed on the  
**surface** of the virion, show sequence variation between serotypes  
and are the sites of interaction with neutralizing antibodies. Virus with  
substitutions in loop I had wild-type growth characteristics, whereas  
virus with substitutions in loop II grew poorly. **Adenoviruses**  
with poliovirus sequences in loop I were recognized and efficiently  
neutralized by antisera specific for the poliovirus sequence; an antiserum  
raised against the **adenovirus** with the poliovirus insert  
specifically recognized the VP1 **capsid** protein of poliovirus  
type 3. It is therefore feasible to alter the **surface**  
properties of the **adenovirus** virion and in doing so to  
manipulate the immune response to this virus.